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EXAMINER	
JOHANNSEN, DIANA B	
ART UNIT	**PAPER NUMBER**
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/775,501	PELTONEN ET AL.	
	Examiner	Art Unit	
	Diana B. Johannsen	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 March 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *41,43,44,48,51,52,56,75-77 and 79-86* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *41,43,44,48,51,52,56,75,77 and 79-86* is/are rejected.

7)☒ Claim(s) *76* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 3, 2010 has been entered.

2. Claims 77 and 83-85 have been amended. Claims 41, 43-44, 48, 51-52, 56, 75-77, and 79-86 remain under consideration. It is noted that applicant's amendment of claim 83 was sufficient to overcome the rejection of that claim under 35 USC 102; however, the claim is now rejected under 35 USC 103. Applicant's arguments have been thoroughly considered and are addressed below following the rejections to which they pertain. Any rejections and/or objections not reiterated herein have been withdrawn. This Office action is non-final.

Election/Restrictions

3. It is again noted that SEQ ID NO: 3 is a non-elected species and remains withdrawn from consideration (see restriction requirement of October 11, 2006 and the modification to a species election in the Office action of January 29, 2007). The original restriction requirement was traversed in the reply of November 13, 2006. The species election was acknowledged but not traversed in the reply of July 27, 2007. Applicant's remarks of March 3, 2010 again note the change from a restriction to a species election,

and include a statement that applicants believe the application is in condition for allowance, such that SEQ ID NO: 3 should be rejoined and examined. However, no generic claim has been allowed in the instant application (in fact, no claims are allowed at the present time). While the examiner concurs that applicant is entitled to consideration of additional species (i.e., SEQ ID NO: 3) upon allowance of a generic claim (as indicated in the action of January 29, 2007), no such claim is allowed at the present time.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 84 and 85 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 84-85 are indefinite because different requirements recited in the claims conflict with one another, rendering the actual structural requirements of the primer(s) encompassed thereby unclear. Particularly, each of the claims requires a "maximum of 24 nucleotides" but also requires a primer that "consists of the sequence selected from the group consisting of SEQ ID NO: 3 and SEQ ID NO:5". While it is clear that SEQ ID NOs 3 and 5 are too large to be considered primers, the manner in which the language "consists of the sequence selected from the group consisting of SEQ ID NO: 3 and SEQ ID NO:5" does limit the claims is not clear, as this recitation appears to literally requiring one of these full length molecules. Accordingly, the combination of different

requirements presently set forth in the claims are contradictory and confusing, rendering the claims indefinite.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 41, 43-44, 48, 51-52, 56, 77, and 79-83 are rejected under 35 U.S.C. 103(a) as being unpatentable over Birren et al (GenBank Accession No. AC016516, April, 2000) in view of Gray et al (US 5,851,769 A [22 December 1998]).

Birren et al disclose the *Homo sapiens* chromosome 2 clone RP11-329I10, which comprises instant SEQ ID NO: 1 (at nucleotides 81,932-82,111; see previously provided alignment), and which also includes a sequence identical to instant SEQ ID NO: 5 with the exception of 3 mismatches (see previously provided alignment). The molecule of

Birren et al does not meet the length limitations of the present claims. However, it is noted that the region of Birren et al's molecule that aligns with instant SEQ ID NO: 1 (nucleotides 81,932-82,111), as well as the sequence identical to SEQ ID NO: 5 except for 3 mismatches, falls within a single contig of 11359 base pairs in length (see the descriptive material appearing before the sequence alignment). The Birren et al reference states that "This is a 'working draft' sequence. It currently consists of 19 contigs. The true order of the pieces is not known and their order in this sequence record is arbitrary". Thus, the Birren et al reference makes clear that the actual order of their contigs has yet to be determined, providing motivation to one of ordinary skill in the art to take further steps to determine that order.

Gray et al disclose methods for the precise physical mapping of genomic DNA (see entire reference). Gray et al teach that their methods provide "an analytic technique to directly map cloned DNA sequences onto individual stretched DNA molecules" (col 14, lines 7-9, as well as col 14 line 52-col 15, line 10) and 'enable absolute physical mapping of one or several cloned probes in the target genomic interval irrespective of their relative positions" (col 15, lines 3-6). Gray et al disclose that their method allows "construction of kilobase resolution physical maps comprised of minimally overlapping cloned DNA sequences" and teaches the use of their methods to rapidly order contigs (see col 16, line 44-col 17, line 64; see also Example 3). In view of the teachings of Gray et al, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the molecule of Birren et al so as to have extracted (via, e.g., restriction digestion) the individual contigs

of Birren et al, including the 11,359 base pair contig taught by Birren et al that contains instant SEQ ID NO: 1, for use – either directly or following amplification or subcloning -- as probes in the methods taught Gray et al, and in doing so, to have produced a nucleic acid molecule meeting the length requirements of the claims. As the Birren et al reference suggests a need to order the contigs of their clone, and as Gray et al teaches that their method may be used to achieve such ordering of contigs, an ordinary artisan would have been motivated to have made such a modification for the advantage of, and to achieve the predictable result of, rapidly ordering the contigs of Birren et al.

With further regard to claims 43-44, a review of the features of the Birren et al clone indicates that the sequence noted above is genomic DNA; thus, the fragments produced as suggested by the teachings of Birren et al in view of Gray et al will also encompass genomic DNA sequences. Regarding claim 44, it is a property of the genomic DNA sequence suggested by Birren et al in view of Gray et al that it includes “part of a gene," as genes are composed of nucleotides.

Regarding claims 48 and 51-52, Gray et al teach subcloning sequences to be mapped (see, e.g., col 17, lines 1-14, as well as col 16, lines 61-63), and teach the use and propagation of a variety of different types of vectors in compatible host cells (see, e.g., col 11, lines 23-39). Accordingly, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have subcloned the contig of Birren et al into any of the vectors/host cells taught by Gray et al, and thereby to have produced vectors and cells meeting the requirements of claims 48 and 51-52, for the

advantage of, and to achieve the predictable result of, successfully preparing subclones for use in the methods suggested by Birren et al in view of Gray et al.

Regarding claim 77 and claims dependent therefrom (56 and 79-82), claim 77 as amended encompasses any nucleic acid molecule "consisting of a sequence of at least 14 consecutive nucleotides of SEQ ID NO: 3, SEQ ID NO: 5, or a complementary sequence thereof, wherein said sequence contains the nucleotide at position 324, and wherein said polynucleotide extends at a maximum 30,000 nucleotides over the 5' and/or 3' end of the nucleic acid molecule of SEQ ID NO:3 and SEQ ID NO:5 or the complementary sequence thereof." The molecule suggested by Birren et al in view of Gray et al, whether in restriction fragment/double stranded probe form or in the form of a subclone or amplicon, includes a complementary sequence meeting the requirements of the claims as written. Accordingly, Birren et al in view of Gray et al suggest a molecule meeting the requirements of claim 77. With further to claim 56, the molecule of Birren et al in view of Gray et al could be employed by one of ordinary skill in the art as a "diagnostic composition", such that the references also suggest claim 56. The body claim 56 defines the complete structure of the claimed product ("comprising the nucleic acid molecule of claim 77"), and the preamble statement of the intended use of "for diagnosing or assessing an individual's predisposition to develop adult-type hypolactasia" is therefore not accorded any patentable weight (see MPEP 2111.02). Regarding claim 79, as the claim is further limiting of the "sequence" of claim 77 (not of the molecule of claim 77), the molecule suggested by Birren et al in view of Gray et al also meets the requirements of claim 79. Regarding claims 80-82, Gray et al further

teaches the labeling of molecules to be used as probes in a variety of ways, including both radioactive and fluorescent labels (see, e.g., col 7, lines 25-58, as well as the preferred embodiments discussed at col 21, lines 25-45 and the Examples). As labeled probes are employed in the mapping methods of Gray et al, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have labeled the probes suggested by Birren et al in view of Gray et al using any of the label types taught by Gray et al to allow for the use of the probes in the ordering of contigs as suggested by the references.

With further regard to claim 83, the is drawn to a "purified or isolated polynucleotide of at least 20 nucleotides the complementary strand of which hybridizes under highly stringent conditions to the nucleic acid molecule selected from the group consisting of SEQ ID NO: 3 or SEQ ID NO: 5, wherein said polynucleotide contains the nucleotide at position 324 of SEQ ID NO: 3 or SEQ ID NO: 5, and wherein said polynucleotide extends at a maximum 30,000 nucleotides over the 5' and/or 3' end of the nucleic acid molecule of SEQ ID NO:3 and SEQ ID NO:5 or the complementary sequence thereof". SEQ ID NO: 5 corresponds to the species elected herein. It is noted that the claimed molecule merely requires "at least 20 nucleotides" wherein the complementary strand "hybridizes under highly stringent conditions" and wherein the polynucleotide "contains the nucleotide at position 324 of" SEQ ID NO: 5. Birren et al disclose the *Homo sapiens* chromosome 2 clone RP11-329I10, which includes a sequence identical to instant SEQ ID NO: 5 with the exception of 3 mismatches (see previously provided alignment). The sequence taught by Birren et al includes position

324 and hundreds of nucleotides of flanking sequence on either side thereof (see sequence alignment); thus, one of ordinary skill in the art would readily recognize that the complementary strand in Birren et al's clone would hybridize with SEQ ID NO: 5 under the conditions required by the claim (it is noted that the claim is not drawn to, e.g., a method employing the recited conditions; rather, the molecule must possess the property set forth in the claim). Further, "the nucleotide at position 324" of instant SEQ ID NO: 5 is present in the molecule of Birren et al, and the combined teachings of Birren et al and Gray et al suggest molecules of lengths embraced by the claim as amended. Thus, the combined teachings of Birren et al and Gray et al suggest the claimed invention.

The response of March 3, 2010 traverses the rejection on the following grounds. The reply argues that Gray et al teach methods of ordering clones, but not methods of determining the order of contigs. The reply urges that Gray et al "merely teaches how to map overlapping clones onto a contig sequence, but fails to contemplate any method for assembling a group of non-overlapping contigs in their true order". The reply further urges that Gray et al does not teach the specific molecules comprising SEQ ID NO: 1 that are required by the claims, and does not teach "hypolactasia nor the association of the specific SNP as is currently claimed".

These arguments have been thoroughly considered but are not persuasive. First, it is acknowledged that (as was indicated in the rejection) Gray et al teach the mapping of clones to order contigs. However, an ordinary artisan would have readily recognized that the methods of Gray et al could be employed to accomplish the

ordering suggested by Birren et al, i.e., to establish the relative positions of the contigs in Birren et al's "working draft" sequence. It is the combined teachings of the references that suggest the molecules of the claims (not the teachings of Gray et al alone). Second, it is noted that the rejection does not assert or allege that Gray et al teaches molecules comprising SEQ ID NO: 1, etc.; rather, it is the combined teachings of Birren et al and Gray et al that suggest the claimed invention. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Finally, regarding the "predisposition to develop adult-type hypolactasia," as is recited in, e.g., claim 56, the examiner concurs that the cited references do not suggest such an association. However, the claim is drawn to a particular product having a specific structure that is defined in the claims. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). See also MPEP 2111.02. While applicant's argument might be persuasive with regard to, e.g., a method in which a variant were detected as an indicator of disease, the instant claims are directed to products that are in fact suggested by the prior art. It is further noted that the claims

require only a single variant molecule (not, e.g., a combination of probes wherein each probe detects one variant), and that the variant claimed is taught by Birren et al.

9. Claims 75 and 86 are rejected under 35 U.S.C. 103(a) as being unpatentable over Birren et al in view of Gray et al, as applied to claims 41, 43-44, 48, 51-52, 56, 77, and 79-83, above, and further in view of Ahern (The Scientist 9:20 [1995]).

The molecules suggested by Birren et al in view of Gray et al are described in the preceding paragraph. The Birren et al and Gray et al references do not teach packaging the molecules suggested by the references into kits, as required by the claims.

Ahern teaches that premade reagents provided in kit form are convenient and save researchers time and money (see p. 3/5-4/5). In view of the teachings of Ahern, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the invention of Birren et al in view of Gray et al so as to have packaged the molecules suggested by the references into a kit. An ordinary artisan would have been motivated to have made such a modification in order to have provided the molecules to practitioners in a convenient format for the advantages of efficiency and cost-effectiveness.

The response traverses this rejection on the grounds that "there is simply no teaching of hypolactasia nor the association of the specific SNPs as is currently claimed". This argument has been thoroughly considered but is not persuasive for the same reason given in the preceding paragraph with regard to the weight accorded the intended use of a product. As the intended use is not sufficient to differentiate the

claimed invention from the molecules suggested by the prior art, applicant's arguments are not persuasive.

10. Claims 84-85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Birren et al in view of Gray et al, as applied to claims 41, 43-44, 48, 51-52, 56, 77, and 79-83, above, and further in view of O'Neill et al (US 6,124,092 [26 Sept 2000]).

It is again noted that the claims are indefinite for the reasons given above. As primers "consisting of the sequence" of SEQ ID NO: 5 are too long to function as primers, the claims have been interpreted herein as being encompassing smaller fragments of SEQ ID NO: 5 that would reasonably be expected by one of ordinary skill in the art to function as primers in an amplification reaction.

The molecules suggested by Birren et al in view of Gray et al are described in the preceding paragraph. The Birren et al and Gray et al references do not teach a primer or primer pair as in claims 84-85. However, it is again noted that Birren et al teach that their sequence is a "working draft" sequence (see Comment section in provided alignment with Accession No. AC016516). Thus, the teaching of Birren et al suggest the need to do additional, confirmatory sequencing of their contigs. Additionally, Gray et al disclose the use of PCR in producing the probes for use in mapping (see, e.g., col 21, lines 24-26). Thus, the Gray et al reference also provides motivation to use PCR in amplifying the contig sequences of Birren et al for use as mapping probes.

O'Neill et al disclose rapid methods for generating and sequencing amplification products (see entire reference, particularly, e.g., col 2, line 64-col 4, line 53). O'Neill et al disclose the use of primers capable of specifically hybridizing to target sequences

that are “typically 18-36 nucleotides in length” (see, e.g., col 6, lines 24-56); such primers are “at least 14 nucleotides” in length, as stated in the present claims, and O’Neill et al thereby also suggest primers 24 nucleotides in length (as such primers fall within the range taught by O’Neill et al) . It is also noted that claims 84-85 merely require that the claimed primer/primer pair "contains the nucleotide at position 324". The primer of claim 84 and the primer pair of claim 85 must "hybridize under highly stringent conditions" to elected SEQ ID NO: 5; however, the claims do not clearly require any particular contiguous portions of that sequence (for example, the claims as written do not require a fragment of SEQ ID NO: 5 that includes nucleotide 324 and particular amounts of flanking sequence).

In view of the teachings of Birren et al, Gray et al and O’Neill et al, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have prepared any primers having the lengths taught by O'Neill et al that could be used in the specific amplification of the molecule suggested by Birren et al in view of Gray et al, and thereby to have produced numerous different primers and primer pairs meeting the requirements of the instant claims. An ordinary artisan would have been motivated to have prepared such primers and primer pairs for the advantage of, and to achieve the predictable result of, confirming the sequence of the contig taught by Birren et al, as suggested by Birren et al's statement that their sequence is a "working draft." Alternatively and/or additionally, an ordinary artisan would have been motivated to have prepared such primers and primer pairs for use in preparing the PCR-amplified probes useful in physical mapping, as suggested by Gray et al.

The response traverses the rejection on the grounds that "There is simply no teaching or suggestion" of the elements of the claim – specifically, of a primer that is "14 to 24 nucleotides in length" and "consists of SEQ ID NOs 3 or 5 (or their complements)" and "contains position 324". These arguments have been thoroughly considered but are not persuasive. It is first noted that the claims have been interpreted as embracing fragments of SEQ ID NO: 5 (as indicated above), such that the references do in fact suggest the molecules claimed. It is also noted that the claims do not in fact require, e.g., a particular fragment of SEQ ID NO: 5 that includes position 324; rather, the claims require a primer that "contains the nucleotide at position 324" (i.e., a C nucleotide). Thus, the references are sufficient to suggest the primer(s) as they are actually being claimed herein.

Conclusion

11. It is again noted that the prior art does not teach or suggest SEQ ID NO: 5. Accordingly, the elected species of claim 76 (i.e., the embodiment directed to an isolated nucleic acid molecule consisting of SEQ ID NO: 5) is free of the art. However, **Claim 76 is objected to as being dependent upon a rejected base claim**. Additionally, the other, non-elected species embraced by claim 76 (SEQ ID NO: 3) remains withdrawn because no generic claim has been allowed in the instant application, as noted above. Particularly, generic claim 41 (from which claim 76 depends) continues to embrace molecules taught in the prior art, as indicated in the above rejection under 35 USC 103.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 571/272-0744. The examiner can normally be reached on Monday-Friday, 8:30 am-2:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached at 571/272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Diana B. Johannsen/
Primary Examiner, Art Unit 1634